PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
SH/TC/34953		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/IB 99/02018	26/11/1999	27/11/1998
Applicant		
LUDWIG INSTITUTE FOR CANCER RESEARCH et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [X] contained in the international application in written form.

   [X] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [X] **Certain claims were found unsearchable** (See Box I).

3. [X] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [ ] the text is approved as submitted by the applicant.

   [X] the text has been established by this Authority to read as follows:

   MAGE-10 OR MAGE-8 DERIVED HLA-A2.1-BINDING OLIGOPEPTIDES

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

   [ ] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [X] None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB 99/02018

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim is 39 directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [X] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [X] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[X] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-11 and 13-39 partially, and 12 completely

   Polypeptides comprising an unbroken sequence from seq.ID.1, either capabale of binding HLA-A2 or of eliciting an immune response from human lymphocytes, nucleic acids encoding them, expression vectors comprising said nucleic acids, hosts comprising said vectors, agents capable of specifically binding said polypeptides, pharmaceutical compositions of said polypeptides, optionally in combination with said HLA, said vector, said host or said binding agent, a cell pulsed with said polypetide presenting it on said HLA on its surface, method of diagnosis using said binding aganet or said nucleic acid, and a method of producing a CTL culture using said polypeptide and said HLA.

   Seq.ID's 43 and 45, derived from seq.ID.2, have been searched with this invention due to their similarity with seq.ID's 42 and 44, respectively.

2. Claims: 1-11, 13-39, all partially

   Polypeptides comprising an unbroken sequence from seq.ID.2, either capabale of binding HLA-A2 or of eliciting an immune response from human lymphocytes, nucleic acids encoding them, expression vectors comprising said nucleic acids, hosts comprising said vectors, agents capable of specifically binding said polypeptides, pharmaceutical compositions of said polypeptides, optionally in combination with said HLA, said vector, said host or said binding agent, a cell pulsed with said polypetide presenting it on said HLA on its surface, method of diagnosis using said binding aganet or said nucleic acid, and a method of producing a CTL culture using said polypeptide and said HLA.

   Seq.ID's 43 and 45 have been searched with the first invention.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1,2,5-7, and 10-39 relate to an extremely large number of possible polypeptides, defined by reference to a desirable characteristic or property, namely their ability to form a complex with an HLA-A2 type molecule and/ or their ability to elicit an immune response.
The claims contain so many possible permutations that a lack of clarity (and/or conciseness) within the meaning of Article 6 PCT arises. Furthermore, the claims cover all polypeptides having the desired characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such polypeptides. In the present case, the claims so lack support, and the application so lacks disclosure, clarity and conciseness, that a meaningful search over the whole of the claimed scope is impossible.
Furthermore, the claims contain so many possible permutations that a lack of clarity (and/or conciseness) within the meaning of Article 6 PCT arises. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the polypeptides by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the nonapeptides defined by claim 3, and larger polypeptides comprising said nonapetidic sequences, e.g. the decapeptides of claim 9.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB 99/02018

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/12 C07K14/47 C07K14/705 C07K7/06 C07K16/18
A61K31/70 A61K38/08 A61K35/14 A61K38/17 G01N33/53

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K C12N A61K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 686 068 A (BOON-FALLEUR THIERRY ET AL) 11 November 1997 (1997-11-11) seq.ID's 31,32 and 57 and the claims tables 1,2	1-3,5-7, 10,11, 13-20, 23,29,30
X	VISSEREN, M.J.W. ET AL.: "Identification of HLA-A*0201-resticted CTL epitopes encoded by the tumor-specific MAGE-2 gene product." INTERNATIONAL JOURNAL OF CANCER, vol. 73, no. 1, 26 September 1997 (1997-09-26), pages 125-30, XP000914539 table 1, peptide entry under "M2 181-189"	1-3,5,6, 10,11, 13-21, 23,29,30

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

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Date of the actual completion of the international search	Date of mailing of the international search report
8 June 2000	27. 06. 00
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Authorized officer Smalt, R

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Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	CHEN, Y.-T. ET AL.: "Identification of multiple cancer/testis antigens by allogenic antibody screening of a melanoma cell line library." PROC.NAT'L.ACAD.SCI.USA, vol. 95, June 1998 (1998-06), pages 6919-23, XP002132946 page 6921, right-hand column, paragraph 3 - paragraph 4; figure 2 ---	1,2,5,6, 12-18, 20,21,23
X	WO 92 20356 A (LUDWIG INST CANCER RES) 26 November 1992 (1992-11-26) whole document, particularly seq.ID.'s 9,20 and 22 and the claims. claims 47,56,101,123,126 ---	1,2,5, 10-26, 29,30, 34,35,39
X	WO 98 14463 A (LUDWIG INST CANCER RES) 9 April 1998 (1998-04-09) see the whole document, particularly example 11. the whole document ---	2,12,13, 15-17, 25,26, 29,34, 35,39
A	RAMMENSEE H -G ET AL: "MHC LIGANDS AND PEPTIDE MOTIFS: FIRST LISTING" IMMUNOGENETICS,DE,SPRINGER VERLAG, BERLIN, vol. 41, no. 4, 1 February 1995 (1995-02-01), pages 178-228, XP000673045 ISSN: 0093-7711 cited in the application the whole document ---	3
A	WO 95 25530 A (UNIV LEIDEN ;LUDWIG INST CANCER RES (US)) 28 September 1995 (1995-09-28) the whole document ---	
P,X	HUANG, L.-Q. ET AL.: "Cytolytic T lymphocytes recognize an antigen encoded by MAGE-A10 on human melanoma." JOURNAL OF IMMUNOLOGY, vol. 162, 1 June 1999 (1999-06-01), pages 6849-54, XP002132947 the whole document ---	1-39
P,X	WO 99 54738 A (LUDWIG INST CANCER RES) 28 October 1999 (1999-10-28) see seq.ID.1 and claims. --- -/--	1,2,5,6, 12-18, 20,21,23

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 99 45954 A (EPIMMUNE INC) 16 September 1999 (1999-09-16) page 95, 4th row of the table; page 102, 12th row of the table. ---	1-3,6,7, 10,11, 13-17
P,X	RIMOLDI, D. ET AL.: "cDNA and protein characterization of human MAGE-10." INTERNATIONAL JOURNAL OF CANCER, vol. 82, no. 6, 9 September 1999 (1999-09-09), pages 901-7, XP000877098 page 902, right-hand column, paragraph 2 page 907, left-hand column, paragraph 2 -right-hand column, paragraph 2 ---	2,12,13, 15-17, 25,26, 29,34, 35,39
E	WO 99 61916 A (SIDNEY JOHN ;EPIMMUNE INC (US); SOUTHWOOD SCOTT (US); SETTE ALESSA) 2 December 1999 (1999-12-02) see page 42, peptide 39.0390, and page 43, peptide 39.0403 -----	1,2,5,6, 10-17, 25,30

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/IB 99/02018

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5686068 A	11-11-1997	US 5554724 A	10-09-1996
		AU 710887 B	30-09-1999
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		CA 2261579 A	05-02-1998
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		AU 682597 B	09-10-1997
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WO 9814463 A	09-04-1998	US 5908778 A	01-06-1999
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		CN 1239479 A	22-12-1999
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		ZA 9708802 A	09-02-1999
WO 9525530 A	28-09-1995	US 5554724 A	10-09-1996
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		US 6063900 A	16-05-2000
		US 5686068 A	11-11-1997
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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/IB 99/02018

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9954738 A	28-10-1999	AU 3007999 A	08-11-1999
WO 9945954 A	16-09-1999	AU 6465598 A	27-09-1999
WO 9961916 A	02-12-1999	AU 4224499 A	13-12-1999

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